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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/559,874	04/25/2000	Jay Leng	CHEM1100	1721

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EXAMINER	
RAWLINGS, STEPHEN L	

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1642	

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/559,874	LENG, JAY	
	Examiner	Art Unit	
	Stephen L. Rawlings, Ph.D.	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *15 August 2002 and 14 July 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-47,63-68 and 71-73* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-47,63-68 and 71-73* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

13)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

a) ☐ The translation of the foreign language provisional application has been received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *19* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Continued Prosecution Application

1. The request filed on July 29, 2002 for a Continued Prosecution Application (CPA) under 37 CFR 1.53(d) based on parent Application No. 09/559,874 is acceptable and a CPA has been established. An action on the CPA follows.

2. The Office action mailed August 29, 2002 has been vacated.

3. The amendment filed August 15, 2002 is acknowledged and has been entered. Claims 48-62, 69, and 70 have been canceled. Claims 1, 18, 31, and 63 have been amended. Claims 71-73 have been added.

4. The amendment filed July 14, 2003 is acknowledged and has been entered. Claims 1, 18, 31, and 63 have been amended.

It is noted that Applicant voluntarily chose to comply with the revised amendment practice before its compliance became mandatory July 30, 2003. The amendment filed July 14, 2003 is not fully compliant with the revised practice, because claim 30 is not included in the listing of the claims. Nevertheless, in order to expedite prosecution, a notice of non-compliancy has not been mailed. Therefore, in reply to this Office action, Applicant is required to submit either (a) a corrected section of the amendment, listing the claims, including claim 30, the appropriate status identifier (e.g., "Original", "Currently Amended", "Canceled"), and, if still pending, the text of the claim, or (b) a new amendment, including a listing all of the claims with the appropriate status identifiers and the text of all pending claims, as required under 37 CFR § 1.121. For further explanation of the amendment format required, see MPEP § 714.

5. The declaration under 37 CFR § 1.132 by Jay Leng filed July 14, 2003 is acknowledged and has been entered.

6. Claims 1-47, 63-68, and 71-73 are pending in the application and are currently under prosecution.

Grounds of Objection and Rejection Withdrawn

7. Unless specifically reiterated below, the grounds of objection and rejection set forth in the previous Office action mailed October 31, 2001 have been withdrawn.

Response to Declaration Under 37 CFR § 1.132

8. The declaration under 37 CFR § 1.132 by Jay Leng filed July 14, 2003 is sufficient to overcome the rejection of claims 1-47 and 63-68 under 35 USC § 112, first paragraph, which was based upon the insufficiency of the disclosure to enable the skilled artisan to make and/or use the claimed invention for the reasons set forth in the Office action mailed October 31, 2001.

Response to Arguments

9. Applicant's arguments with respect to the rejection of claims 1-47 and 63-68 under 35 USC § 103(a) have been considered but are moot in view of the new grounds of rejection set forth below. The merits of Applicant's arguments with respect to other grounds of rejection or objection, which are reiterated herein, are addressed below.

Specification

10. The disclosure is objected to for the reason set forth in the Office Action mailed October 31, 2001 (Paper No. 9). However, as noted therein, in view of Applicant's expressed willingness to make the deposit and to amend the specification to insert the ATCC accession number, this matter has been set aside until this application is in a condition for allowance except for the needed deposit and amendment to the specification. At that time Applicant will be invited make the deposit and amend the specification. Applicant will be given a period of time within which the deposit must be made in order to avoid abandonment. This time period is <u>not</u> extendable under § 1.136(a) or (b) if set forth in a "Notice of Allowability" or in an Office action having a mail date on or after the mail date of a "Notice of Allowability" (see § 1.136(c)).

Claim Objections

11. Claim 7 is objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. Claim 7 fails to further limit the subject matter of claim 1, because claim 1 is drawn to a method comprising contacting a cell transfected with a polynucleotide encoding *Renilla* luciferase; therefore claim 1 is drawn to a method comprising contacting a cell containing a transgene encoding *Renilla* luciferase. Since claim 7 merely recites, "wherein the cell contains a transgene encoding *Renilla* luciferase", claim 7 does not further limit the subject matter that is encompassed by claim 1.

12. Claim 25 is objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. Claim 25 fails to further limit the subject matter of claim 18, because claim 18 is drawn to a method comprising obtaining data from a cell transfected with a polynucleotide encoding *Renilla* luciferase; therefore claim 18 is drawn to a method comprising obtaining data from a cell containing a transgene encoding *Renilla* luciferase. Since claim 25 merely recites, "wherein the cell contains a transgene encoding *Renilla* luciferase", claim 25 does not further limit the subject matter that is encompassed by claim 18.

13. Claim 71 is objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. Claim 71 fails to further the limit the subject matter of claim 1, because claim 1 is drawn to a method comprising "comparing the light emission data **from the lysate** in the presence of the agent" (emboldened for emphasis). Since measuring the light emitted from the lysate necessarily requires that the cells be lysed, it follows that before the comparison can be made, the cells must be lysed. Therefore, since claim 71 merely recites,

"wherein the lysing is performed prior to comparison of the light emission data", claim 71 does not further limit the subject matter encompassed by claim 1.

14. Claim 72 is objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. Claim 72 fails to further the limit the subject matter of claim 31, because claim 31 is drawn to a method comprising "comparing the light emission data **from the lysate** in the presence of the agent" (emboldened for emphasis). Since measuring the light emitted from the lysate necessarily requires that the cells be lysed, it follows that before the comparison can be made, the cells must be lysed. Therefore, since claim 72 merely recites, "wherein the lysing is performed prior to comparison of the light emission data", claim 72 does not further limit the subject matter encompassed by claim 31.

Claim Rejections - 35 USC § 112

15. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

16. Claims 1-47, 63-68, and 71-73 are rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. The omitted steps are set forth in section 7 of the Office Action mailed March 9, 2001 (Paper No. 7).

It is noted that the present claims have been amended by Applicant to recite a step in which a cellular lysate is prepared. As the claims 1, 31, and 63 recite a step in which light emissions are measured in the presence and absence of an agent, or in which a comparison between the light emission from the lysate in the presence and absence of an agent is made, it is explicit, or at least implicit that light emission data must be collected in the presence and absence of the agent to practice the claimed invention. Therefore, to the extent that the stated rejection was based upon the omission of steps in which a cellular lysate is prepared and in which light emission data is collected in the presence and absence of the agent, the stated grounds of

rejection are moot. The step, which remains omitted, then, is the step in which coelenterazine is added to the lysate.

Applicant has traversed the grounds of rejection arguing that the present claims recite the each and every essential step and that none of the allegedly omitted steps are required to practice the claimed invention. Applicant argues coelenterazine can be added either as the cells are being lysed or after the cells have been lysed, so it would be "incorrect to add a step to the claims that requires that colenterazine must be added to the lysate" (Amendment of August 15, 2002, page 6, paragraph 4)

To the extent that Applicant's arguments address the extent of the stated rejection, which is based upon the omission of steps in which a cellular lysate is prepared and in which light emission data is collected in the presence and absence of the agent, just as the stated grounds of rejection were rendered moot by amendment, Applicant's arguments are moot and will not be addressed. However, as the present claims do not recite a step in which coelenterazine is added to the lysate, the rejection is herein maintained.

In reply to Applicant's argument the allegedly omitted step of adding coelenterazine to the lysate is not essential, because coelenterazine can be added either as the cells are being lysed or after the cells have been lysed, the specification teaches that coelenterazine must be added to the lysate. If coelenterazine were not added, there would be no light emission; the luciferase contained within the lysate will not produce light in the absence of a suitable substrate. The specification teaches only one suitable substrate, namely coelenterazine. While adding coelenterazine while the cells are being lysed, as Applicant has argued, might enable the practice of the invention, luciferase must nevertheless be contacted by coelenterazine. A step in which coelenterzine is added to the luciferase containing sample is essential to the practice the claimed and disclosed invention. Therefore, amending claims 1, 18, 31, and 63 to recite, for example, a step in which coelenterazine is added to the lysate can obviate this ground of rejection.

17. Claims 18-30 and 73 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 18-30 are indefinite because claim 18 does not recite a positive correlation step that clearly relates the method steps recited in the body of the claim to the preamble of the claim. Moreover, as written, the preamble of claim 18 reads, "for determining cell proliferation of a cell or a population of cells", whereas in the last line the claim reads, "wherein a change in light emission data is indicative of a change in cell proliferation". Measuring a change in cell proliferation is not exactly the same as determining whether or not a cell or population of cells is proliferating. Because of the inconsistency of the claim language, the metes and bounds of the subject matter cannot be determined unambiguously.

Claim 73 is indefinite because the claim recites, "prior to comparison of the light emission data". There is no antecedent basis in claim 73 or claim 63 for said comparison.

Claim Rejections - 35 USC § 102

18. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

19. Claims 18, 20, 21, 24, 25, 27, and 28 are rejected under 35 U.S.C. 102(b) as being anticipated by Lorenz et al. (*J. Biolumin. Chemilumin.* 1996 Jan-Feb; **11** (1): 31-37; of record), as evidenced by US Patent No. 5,998,583 A.

At page 9 of the amendment filed August 15, 2002, Applicant states the recitation of intended use in the preamble of claim 18 is not to be considered limiting; therefore, claim 18 is drawn to an *in vitro* method comprising lysing cells expressing a transgene encoding *Renilla* luciferase and measuring light emission produced by the lysate over a period of time to obtain light emission data, wherein a change in light emission data is indicative a change in cell proliferation.

Lorenz et al. teaches a method comprising lysing cells expressing a transgene encoding *Renilla* luciferase and measuring light emission produced by the lysate over a period of time to obtain light emission data; see entire document, particularly the abstract. Lorenz et al. teaches that COS-7 monkey kidney cells or C5 mouse fibroblasts, which are both mammalian and eukaryotic, can be transfected with a nucleic acid molecule encoding *Renilla* luciferase and the cells can be exposed to coelenterazine in culture to acquire light emission data *in vivo*; see, e.g., page 33, columns 1 and 2. Lorenz et al. teaches light emission data can be measured and accumulated for over a period of 5 minutes using a counting tube (page 33, column 2). The COS-7 and C5 cells of Lorenz et al. were obtained from a tissue sample of a mammal, as required by claims 27, 28, and 30.

US Patent No. 5,998,583 A teaches a change a change in cell viability can be estimated as the relative luciferase activity of a culture of cells co-transfected with a luciferase reporter construct and an expression plasmid expressing a protein that affects cell proliferation, as compared with the luciferase activity of a control culture of cells in which the luciferase reporter has been co-transfected with an empty expression plasmid (columns 27-29, Example 5). Accordingly, although Lorenz et al. does not expressly teach that a change in light emission data can be indicative of a change in cell proliferation, as evidenced by the teachings of US Patent No. 5,998,583 A, the relative luciferase activity of a culture of cells is indicative of the number of viable cells in the culture and therefore a change in light emission as measured according to the method of Lorenz et al. can be indicative of a change in cell proliferation.

Claim Rejections - 35 USC § 103

20. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

21. Claims 1, 2, 7, 9-12, 16-19, 24, 25, 31, 32, 40-47, 71, and 72 are rejected under 35 U.S.C. 103(a) as being unpatentable over Virta et al. (*Antimicrobial Agents Chemother.* 1994 Dec; **38** (12): 2775-2779; or record) in view of Lorenz et al. (*J. Biolumin. Chemiliumin.* 1996 Jan-Feb; **11** (1): 31-37; of record).

Virta et al. teaches measuring the luciferase activity of a population of prokaryotic cells transformed with a transgene encoding luciferase cultured in the absence and presence of various concentrations of an agent, where a difference in the luciferase activity of the cell in the presence and absence of the agent is indicative of an effect of the agent upon the proliferation of the cell and its sensitivity, or susceptibility to the agent; see entire document, particularly the abstract. Virta et al. teaches measuring the luminescence over a period time; see, e.g., page 2777, Figure 4. Virta et al. discloses good agreement in the results of two assays used to measure cell numbers and suggests the assay measuring decreased luminescence in the presence of an agent provides a rapid and more sensitive indication of the cytotoxicity of the agent (abstract). Virta et al. discloses the assay can be used to investigate the antimicrobial activities of different compounds, which are antibiotic drugs; see, e.g., page 2778, column 2.

Virta et al. does not teach or suggest using *Renilla* luciferase.

Lorenz et al. teaches that which is set forth above. In addition, Lorenz et al. discloses that *Renilla* luciferase may be superior to other luciferases because it requires no divalent cations, no ATP, and no long-chain aldehydes (page 35, column 2). Furthermore, Lorenz et al. teaches mammalian membrane permeability to coelenterazine does not appear to pose a problem (page 35, column 2).

It would have been *prima facie* obvious to one of ordinary skill in the art at the time of the invention to use a transgene encoding *Renilla* luciferase, rather than firefly luciferase, in practicing the methods of Edinger et al., because Lorenz et al. discloses the suitability and advantages of using *Renilla* luciferase, as opposed to other luciferases. One of ordinary skill in the art at the time of invention would have been motivated to do so to assess the affect of candidate antibiotic agents upon the proliferation of prokaryotic cells.

22. Claims 1, 3-7, 9-18, 20-31, 33-47, 63-68, and 71-73 are rejected under 35 U.S.C. 103(a) as being unpatentable over US Patent No. 5,998,583 A in view of Lorenz et al. (*J. Biolumin. Chemiliumin.* 1996 Jan-Feb; **11** (1): 31-37; of record).

US Patent No. 5,998,583 A ('583) teaches an *in vitro* assay for determining cell proliferation of a cell or population of cells in order to determine the effect of an agent on cell proliferation or to screen mammalian cells to determine their susceptibility to treatment with an agent, wherein said method comprises:

(a) contacting cells transfected with a polynucleotide encoding a luciferase with an agent suspected of modulating cell proliferation;

(b) lysing the cells that have and have not been contacted with the agent to prepare a lysate; and

(c) measuring and comparing light emissions from lysates prepared from the cells in the presence and absence of the agent;

See columns 27-29, Example 5. '583 teaches the agent, namely BID, which is a protein, or a derivative thereof, was suspected of modulating cell proliferation; see, e.g., the abstract. '583 teaches the cells expressing luciferase can be contacted with the agent by expressing the agent within the cell (columns 27-29, Example 5). '583 discloses that a difference in the light emissions of the lysate indicates the viability of the cells in the presence or absence of the agent, which in turn indicates the susceptibility of the cell's viability to the agent and indicates the effect upon the cell's proliferation by the agent (columns 27-29, Example 5). '583 teaches the cells can be lysed before acquiring light emission data (columns 27-29, Example 5). Although '583 shows that the assay can be practiced using cultured rat fibroblasts, '583 suggests the assay can be practiced using Jurkat cells, which are cultured human cancer cells obtained from a

biological sample obtained from a human subject, i.e., a blood or tissue sample; see, e.g., column 27, lines 59-65.

'583 does not explicitly teach or suggest *Renilla* luciferase.

Lorenz et al. teaches that which is set forth above.

It would have been *prima facie* obvious to one of ordinary skill in the art at the time of the invention to use *Renilla* luciferase in practicing the methods of '583, because Lorenz et al. discloses the suitability and advantages of *Renilla* luciferase and teaches luminescence data can be collected using intact cells, obviating the need to first prepare a cell lysate. Although '583 does not expressly teach or suggest repeating the process with a second agent after washing the cells, it would have been *prima facie* obvious to one ordinarily skilled in the art to wash the cells before contacting the cells with a second agent and measuring the effect of adding the second agent by measuring the luminescence produced by the cells. One of ordinary skill in the art at the time of the invention would have been motivated to do so to monitor the effects of BID and other modulators of cell proliferation, because '583 teaches a change in the luciferase activity of the cell over time is indicative of a change in viable cell number and demonstrates the utility of a luciferase-based assay to assess proliferation in order to determine the effect of an agent suspected of modulating the proliferation of the cells.

Double Patenting

23. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

24. Claims 1-47, 63-68, and 71-73 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-47 and 63-68 of copending Application No. 09/586,339 in view of Zhang et al. (*Clin. Exp. Metastasis.* 1994 Mar; **12** (2): 87-92) and Lorenz et al. (*J. Biolumin. Chemiliumin.* 1996 Jan-Feb; **11** (1): 31-37; of record).

The claimed inventions of the copending applications differ in that the claimed invention of 09/586,339 is practiced using intact cells, whereas the present claims require the method to be practiced *in vitro* using a cell lysate. Zhang et al. teaches that luciferase activity of cells transfected with a gene encoding luciferase can be measured using either a cell lysate or an intact cell and that independently of the method used to measure the activity, the activity correlates with the viable cell number and can be used as an indication of the effect of an agent upon the proliferation of the cells. Lorenz et al. teaches the luciferase activity of cells transfected with a gene encoding *Renilla* luciferase can be measured *in vitro* using either a cell lysate or an intact cell. Therefore, in view of the prior art, although the conflicting claims are not identical, they are not patentably distinct from each other under the judicially created doctrine of obviousness-type double patenting.

This is a provisional obviousness-type double patenting rejection.

Conclusion

25. No claims are allowed.

26. The prior art made of record and not relied upon is considered pertinent to applicant's disclosure. US Patent No. 6,638,752 B2 teaches the constitutive expression of a transgene encoding *Renilla* luciferase can be used as a marker to track viability. Sharif et al. teaches an assay for examining the anti-proliferative effects of agents against cells expressing luciferase. Coombe et al. teaches a luciferase assay for measuring the cell growth and viability. Naylor reviews the reporter gene technology and teaches the suitability of *Renilla* luciferase. Kramer et al. teaches a luciferase assay for determining the effects of an agent on a cell transfected with a gene expressing luciferase. Inouye et al. teaches the versatility and advantages of using *Renilla* luciferase, as opposed to firefly luciferase. Sweeney et al. teaches HeLa cells transfected with a gene encoding a luciferase can be used to assess the effect of an agent upon proliferation of the cells by measuring luciferase activity in the presence and absence of one or more agents, and that decreased luminescence in the presence of an agent provides an indication of reduced tumor load and of the cytotoxicity of the agent. Demirpence et al. teaches an assay measuring luciferase activity of a population of intact cells, which after the assay can be cultured *de novo* by simply replacing the reaction medium with a fresh culture medium so that the cells can later be used again. Contag et al. teaches the luciferase activity of transfected cells can be measured *in vivo*; furthermore, Contag et al. teaches the transfected cells can be removed from the body and used *ex vivo*.

27. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Stephen L. Rawlings, Ph.D. whose telephone number is (571) 272-0836. The examiner can normally be reached on Monday-Friday, 8:30AM-5:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (571) 272-0841. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Stephen L. Rawlings, Ph.D.
Examiner
Art Unit 1642

slr
June 21, 2004

CHRISTINA CHAN
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600